UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
08/822,033	03/24/1997	WAYNE A. MARASCO	43471-FWC	5884

7590 05/31/2006

Ronald I. Eisenstein
NIXON PEABODY LLP
101 Federal Street
Boston, MA 02110

EXAMINER
WOITACH, JOSEPH T

ART UNIT	PAPER NUMBER
1632	

DATE MAILED: 05/31/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	08/822,033	MARASCO ET AL.	
	Examiner	Art Unit	
	Joseph T. Woitach	1632	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *21 March 2006*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1 and 3-17* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1 and 3-17* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *2/22/1994* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

This application is a file wrapper continuation of 08/199, 070, filed February 22, 1994.

Applicants' amendment filed March 21, 2006 has been received and entered. Claim 1 has been amended. Claim 2 has been cancelled. Claims 1, 3-17 are pending and currently under examination.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1, 5-7 rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention is withdrawn.

Initially, it is noted that the amendments to the claims has obviated the specific basis of the previous rejection. The present claims find literal and figurative support in the instant disclosure. In addition to figure 2 and pages 25-26 of the examples relied upon by Applicants, it is noted that on page 14 a description for making vectors that encode antibody/DNA binding fusion proteins is disclosed.

Claim Rejections - 35 USC 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 1, 3-5, 7-17 stand rejected under 35 U.S.C. 103(a) as being unpatentable over Beug *et al.*, Chaudhary *et al.* and Wu *et al.* for the reasons below and as set forth in the previous office action.

Initially, it is noted in response to Applicants comments on the last page of the amendment that claim 17 was not rejected, review of the last office action clearly states that claim 17 was rejected in the above rejection. It may have been overlooked by Applicants because it was a new claim that was newly rejected in the form paragraph, however it is clearly part of the rejection. Moreover, it is noted that claim 17 is broader than the specific species of RNA set forth in claim 8, and the rejection of this broader claim is consistent with the previous rejection and its merits are addressed/discussed in the basis of the rejection in light of the teaching of Wu.

Applicants argue that the specification provides a disclosure that the claimed fusion protein provides high binding activity and a superior delivery method as compared to the prior art. Applicants note that the present disclosure provides support that presently claimed composition versus a chemically linked composition provides for "potentially better binding activity" citing page 39 of the specification (Applicants amendment page 7 of 8). This is not found persuasive. The comparison is noted, however, it is not unexpected that the somewhat harsh conditions of certain cross-linking method would result in non-functional proteins as well as possible cross-linking that result in a steric hindrance of the variable region of an antibody. Further, while not bolded in Applicants arguments and citation the specification clearly states that the there is "**potentially** better binding", as it would be recognized by the skilled artisan that the activity of the resulting protein would depend on various factors for making fusion proteins as well as inherent problems/properties of the fusion protein itself.

It is argued that using antibodies instead of receptors as a targeting moiety provides for a more selective targeting, noting that Wu and Beug each teach the use of receptors. This is not found convincing because Wu does teach to use antibodies and antibody fragments (see starting on top of page 6 for example). Further, while the specific working examples may have used receptors as targeting moieties, the artisan would appreciate that restricting to the use of receptors alone is limited by the knowledge of a receptor/ligand combination that is useful and specific for targeting. The disclosures as a whole (for example Wu) provide for targeting any cell surface molecule/antigen and would clearly require the use of other targeting moieties such as antibodies.

Finally, it is argued that embodiments of delivering RNA as set forth in claim 17 are not taught in the references, and that delivery of RNA as taught by Rossi *et al.* is difficult. This is not found convincing because Wu does provide a teaching for the delivery of RNA, in particular the use of mRNA and ribozymes. Arguments related to the teachings of difficulties highlighted by Rossi *et al.* are not found on point because they are directed to problems of delivering naked RNA, not the use of other compositions for delivery and/or targeting. Further, such arguments only apply to one intended use, and as recognized by Rossi *et al.* such problems are not apparent when delivery is to cells *in vitro* (page 683, first full paragraphs in first column).

Applicants' arguments have been fully considered, but not found persuasive. As noted previously, Applicants arguments focus primarily on the assertion that a recombinantly made protein would be more effective than one made chemically. At the time of filing, Applicants do not dispute that fusion protein can be made (noting that Wu prefers the use of a peptide bond as a linker p. 8), that fusion proteins were used to deliver polynucleotides, it is only contested that a recombinantly made fusion protein would be superior to one that was produced chemically. Given the evidence of record and in view of the breadth of the claims for a recombinant fusion protein made by any means (i.e. in cells that would not make an active or secreted form that would require re-folding for example), Applicants arguments of the superiority of the claimed system over that made obvious by the cited art is not found convincing.

Wu *et al.* provide evidence that a targeting molecule was fused to nucleotide binding agents such as polylysine, polyarginine, polyornithine, as well as other DNA binding protein known in the art such as hisotones, avidin, and protamines, though the Examiner acknowledges

that the linkage was done chemically (page 7, bottom of the page). Here, Wu *et al.* clearly teach the combination of a cell targeting protein with a nucleotide binding molecule as one fusion protein. Because Wu *et al.* does not teach a chemical linkage that would result in the same fusion protein as one made recombinantly, the reference can not be used as anticipatory reference in a 102 type rejection. However, it does provide clear evidence that fusion proteins comprising the two protein elements recited in claim 1(a) were made and used to deliver polynucleotides (claim 1(b) limitation) at the time of filing. Thus, it is maintained that at the time of filing the use of fusion proteins for the delivery of polynucleotides was known. The methodology used to generate a fusion protein is that known and conventional in the art at the time of filing (also acknowledged by the instant specification). Chaudhary *et al.* has been cited to substantiate the statements in the instant specification regarding the technology of making recombinant fusion proteins. Moreover, Chaudhary *et al.* provides teaching for specific embodiments in the claims and a clear expectation of success for the use of recombinant technology in making fusion proteins. Examiner acknowledges that Chaudhary *et al.* does not teach nor provide the specific motivation to deliver a polynucleotide in the teachings, however this is not why Chaudhary *et al.* is cited. The specific motivation to combine the teachings of the cited references comes from Beug *et al.* who teach fusion proteins for the delivery of polynucleotides, and that any method could be used to generate the fusion protein and specifically suggest recombinant technology. Similar to Wu *et al.* Beug *et al.* teach that when the peptides are coupled, for example a ligand to polylysine, and importantly that recombinant methods can be used to generate the recombinant protein (see for example page 7). Applicants' previous arguments that the combined references provide only for chemical linkage, is not

persuasive because fusion proteins comprising two protein portions, one comprising a targeting moiety and one that binds a polynucleotide, were known in the art at the time of filing, and the cited references give specific suggestion to use methods known in the art such as generating them recombinantly.

Therefore, for the reasons above and of record, the rejection is maintained.

Claim 6 stands rejected under 35 U.S.C. 103(a) as being unpatentable over Beug *et al.*, Chaudhary *et al.* and Wu *et al.* as applied to claims 1, 3-5, 7-16 above, and in further view of Ryder *et al.* for the reasons below and as set forth in the previous office action.

Applicants argue that the teaching of Ryder *et al.* does not overcome the essential deficiency of Beug *et al.*, Chaudhary *et al.* and Wu *et al.* as discussed for claims 1, 3-5, 7-16. See Applicants' amendment, page 8 of 8. Applicants' arguments have been fully considered, but not found persuasive.

As reasoned above, Beug *et al.*, Chaudhary *et al.* and Wu *et al.* provide the necessary teaching and motivation to make obvious claims 1, 3-5, 7-17. Beug *et al.* and Wu *et al.* teach that any variety of polynucleotide binding sequences can be used in forming the complexes and and attached to the targeting moiety, however specific polynucleotide sequences are not taught. Ryder *et al.* is relied upon to teach that at the time of filing among the various species of sequences recited in claim 6, the Jun DNA binding sequences were known. As noted in the previous office action, Ryder *et al.* is not relied upon to correct deficiencies of Beug *et al.*, Chaudhary *et al.* and Wu *et al.*, rather the teachings are relied upon to teach what was known in the art at the time of filing. Ryder *et al.* provide a detailed teaching for the specific DNA binding

sequences and demonstrate that they are effective in binding target DNA as evidenced by the gel shift assay (see results in figure). Applicants= arguments are unpersuasive because Beug *et al.*, Chaudhary *et al.* and Wu *et al.* provide the necessary teaching to make obvious claims 1, 3-5, 7-17, and claim 6 is obvious in light of the teaching of Ryder *et al.* for the specific c-jun DNA binding sequences.

Therefore, for the reasons above and of record, the rejection is maintained.

Conclusion

No claim is allowed.

THIS ACTION IS MADE FINAL. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Joseph Woitach whose telephone number is (571) 272-0739.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ram Shukla, can be reached at (571) 272-0735.

Any inquiry of a general nature or relating to the status of this application should be directed to the Group analyst Dianiece Jacobs whose telephone number is (571) 272-0532.

Joseph T. Woitach

Joe Woitach
AU1632